

That which is claimed:

1. A device for acoustically ejecting a fluid droplet toward a designated site on a substrate surface, comprising:
  - (a) a reservoir adapted to contain a fluid and enabling conduction of acoustic energy in a substantially uniform manner; and
  - (b) an ejector comprised of an acoustic radiation generator for generating acoustic radiation and a lens capable of focusing the generated acoustic radiation to emit a droplet from a surface of a fluid contained within the fluid reservoir, said ejector having an f-value of greater than 2.
2. The device of claim 1, further comprising:
  - (c) a means for positioning the ejector (i) in acoustic coupling relationship to the reservoir.
3. The device of claim 2, comprising a plurality of reservoirs each adapted to contain a fluid, and wherein the device is capable of ejecting a fluid droplet from each of the plurality of reservoirs toward a plurality of designated sites on the substrate surface.
4. The device of claim 3, wherein each of the reservoirs is removable from the device.
5. The device of claim 3, wherein each reservoir comprises an individual well in a well plate.
6. The device of claim 5, wherein the well plate contains at least 96 wells.
7. The device of claim 5, wherein the well plate contains between about 96 to about 1500 reservoirs.
8. The device of claim 5, wherein the well plate contains at least 1536 wells.

9. The device of claim 5, wherein the well plate contains thousands of wells.
10. The device of claim 5, wherein the well plate contains many thousands of reservoirs.
11. The device of claim 3, wherein the reservoirs are arranged in an array.
12. The device of claim 3, wherein the reservoirs are substantially acoustically indistinguishable.
13. The device of claim 3, wherein the reservoirs comprise a portion of a micro-titer plate.
14. The device of claim 3, wherein at least one of the reservoirs is adapted to contain no more than about 2000 nanoliters of fluid.
15. The device of claim 3, wherein at least one reservoir contains a fluid.
16. The device of claim 15, wherein each reservoir contains a different fluid.
17. The device of claim 15, wherein at least one of the reservoirs contains an aqueous fluid.
18. The device of claim 15, wherein at least one of the reservoirs contains a nonaqueous fluid.
19. The device of claim 15, wherein at least one of the reservoirs contains two substantially immiscible fluids.
20. The device of claim 18, wherein the nonaqueous fluid comprises an organic solvent.

21. The device of claim 18, wherein the nonaqueous fluid comprises a non-biological fluid.

22. The device of claim 15, wherein at least one of the fluid containing reservoirs contains a biomolecule.

23. The device of claim 15, wherein at least one of the fluid containing reservoirs contains a chemical or biological compound.

24. The device of claim 23, wherein the biomolecule is selected from the group consisting of nucleotides, peptides, oligomers, and polymers.

25. The device of claim 23, wherein the biomolecule is attached to a cell.

26. The device of claim 3, wherein the positioning means is adapted to repeatedly reposition the ejector so to enable ejection of a droplet from each of the reservoirs.

27. The device of claim 26, further comprising a substrate positioning means for positioning the substrate surface with respect to the ejector.

28. The device of claim 3, further comprising a means for maintaining a fluid in each reservoir at a constant temperature.

29. The device of claim 3, further comprising a temperature controlled coupling fluid provided between the ejector and each reservoir.

30. The device of claim 3, comprising a single ejector.

31. The device of claim 2, wherein the acoustic coupling relationship comprises positioning the ejector such that the acoustic radiation is generated and focused external to the reservoir.

32. The device of claim 31, wherein the acoustic coupling relationship between the ejector and the fluid in the reservoir is established by providing an acoustically conductive medium between the ejector and the reservoir.

33. The device of claim 1, wherein said f-value is greater than approximately 3.

34. The device of claim 1, wherein said f-value is no more than 4.

35. The device of claim 1, wherein said f-value is in the range of approximately 2.5 to approximately 3.

36. The device of claim 1, wherein said f-value is approximately 4.

37. The device of claim 1, comprising more than one thousand reservoirs.

38. The device of claim 1, comprising thousands of reservoirs.

39. The device of claim 1, comprising many thousands of reservoirs.

40. The device of claim 1, further comprising cooling means for lowering the temperature of the substrate surface.

41. A method for ejecting a fluid from a fluid reservoir toward designated sites on a substrate surface, comprising:

(a) providing a device comprised of:

(i) a reservoir containing a first fluid and enabling conduction of acoustic energy in a substantially uniform manner, and

(ii) an ejector comprised of an acoustic radiation generator for generating acoustic radiation and a lens capable of focusing the generated acoustic radiation to emit a droplet from a surface of the first fluid contained within the fluid reservoir, said ejector having an f-value of greater than 2;

(b) positioning the ejector so as to be in acoustically coupled relationship to the fluid-containing reservoir;

(c) activating the ejector to generate acoustic radiation, thereby ejecting a droplet of the first fluid from the reservoir.

42. The method of claim 41, wherein said f-value is greater than approximately 3.

43. The device of claim 41, wherein said f-value is in the range of approximately 2.5 to approximately 3.

44. The method of claim 41, wherein said f-value is no more than 4.

45. The method of claim 41, wherein said f-value is approximately 4.

46. The method of claim 41, wherein the ejected droplet has a diameter less than the diameter of a focal spot of the acoustic radiation at the surface of the first fluid.

47. The method of claim 46, wherein two droplets are ejected during step (c).

48. The method of claim 47, wherein the two ejected droplets are deposited as first and second droplets and the second droplet is larger than the first droplet.

49. The method of claim 47, wherein each of the ejected droplets has a width less than the diameter of the focal spot.

50. The method of claim 41, wherein the device comprises a plurality of reservoirs each adapted to contain a fluid, and wherein the device is capable of ejecting a fluid droplet from each of the plurality of reservoirs toward a plurality of designated sites on the substrate surface and the method further comprises:

(d) positioning the ejector so as to be in acoustically coupled relationship to a second fluid-containing reservoir containing a second fluid; and

(e) activating the ejector as in step (b) to eject a droplet of the second fluid from the second reservoir toward a second designated site on the substrate surface.

51. The method of claim 50, wherein each of the ejected droplets of the first fluid and second fluids has a width less than the diameter of a focal spot of the acoustic radiation at the surface of the first fluid.

52. The method of claim 50, wherein two droplets are ejected during at least one of steps (c) or (e).

53. The method of claim 52, wherein each of the two droplets ejected during step (c) or (e) has a width less than the diameter of a focal spot of the acoustic radiation at the surface of the first fluid.

54. The method of claim 52, wherein at least two ejected droplets are deposited at the same designated site on the substrate surface.

55. The method of claim 54, wherein the two ejected droplets are deposited as first and second droplets and the second droplet is larger than the first droplet.

56. The method of claim 50, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet size and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet of the desired size.

57. The method of claim 50, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet velocity and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet at the desired droplet velocity.

58. The method of claim 50, further comprising repeating steps (d) and (e) with one or more additional fluid-containing reservoirs.

59. The method of claim 50, wherein each of the ejected droplets has a volume of 5 pL.

60. The method of claim 50, wherein each of the ejected droplets has a diameter in the range of about 30 micrometers to about 60 micrometers.

61. The method of claim 50, wherein each of the ejected droplets has a diameter in the range of about 120 micrometers to about 250 micrometers.

62. The method of claim 50, wherein each of the ejected droplets has a diameter in the range of about 60 micrometers to about 500 micrometers.

63. The method of claim 50, wherein each of the ejected droplets has a diameter in the range of about 500 micrometers to about 1,000 micrometers.

64. The method of claim 50, wherein each of the ejected droplets has a diameter in the range of about 1 micrometer to about 10,000 micrometers.

65. The method of claim 50, wherein each of the ejected droplets has a diameter of less than about 10,000 micrometers.

66. The method of claim 50, further comprising, before each ejector activation step, measuring the fluid level in the reservoir in acoustically coupled relationship with the ejector.

67. The method of claim 66, wherein each measuring step is carried out acoustically.

68. The method of claim 67, wherein each measuring step is carried out using acoustic radiation from the ejector.

69. The method of claim 41, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet size and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet of the desired size.

70. The method of claim 41, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet velocity and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet at the desired droplet velocity.

71. A device for acoustically ejecting a fluid droplet toward a designated site on a substrate surface, comprising:

(a) a reservoir adapted to contain a fluid and having an aperture that enables conduction of acoustic energy in a substantially uniform manner, said aperture having a selected cross-sectional width; and

(b) an ejector comprised of an acoustic radiation generator for generating acoustic radiation and a focusing means capable of focusing the generated acoustic radiation to emit a droplet from a surface of a fluid contained within the fluid reservoir said surface being an effective distance from the aperture,

wherein the ratio of the effective distance to the cross-sectional width of the aperture is greater than about 2:1.

72. The device of claim 71, further comprising:

(c) a means for positioning the ejector (i) in acoustic coupling relationship to the reservoir.

73. The device of claim 72, comprising a plurality of reservoirs each adapted to contain a fluid, and wherein the device is capable of ejecting a fluid droplet from each of the plurality of reservoirs toward a plurality of designated sites on the substrate surface.



74. The device of claim 73, wherein each of the reservoirs is removable from the device.

75. The device of claim 73, wherein each reservoir comprises an individual well in a well plate.

76. The device of claim 75, wherein the well plate contains at least 96 wells.

77. The device of claim 75, wherein the well plate contains between about 96 to about 1500 reservoirs.

78. The device of claim 75, wherein the well plate contains at least 1536 wells.

79. The device of claim 75, wherein the well plate contains thousands of wells.

80. The device of claim 75, wherein the well plate contains many thousands of reservoirs.

81. The device of claim 73, wherein the reservoirs are arranged in an array.

82. The device of claim 73, wherein the reservoirs are substantially acoustically indistinguishable.

83. The device of claim 73, wherein the reservoirs comprise a portion of a micro-titer plate.

84. The device of claim 73, wherein at least one of the reservoirs is adapted to contain no more than about 2000 nanoliters of fluid.

85. The device of claim 73, wherein at least one reservoir contains a fluid.

86. The device of claim 85, wherein each reservoir contains a different fluid.
87. The device of claim 85, wherein at least one of the reservoirs contains an aqueous fluid.
88. The device of claim 85, wherein at least one of the reservoirs contains a nonaqueous fluid.
89. The device of claim 85, wherein at least one of the reservoirs contains two substantially immiscible fluids.
90. The device of claim 89, wherein the nonaqueous fluid comprises an organic solvent.
91. The device of claim 89, wherein the nonaqueous fluid comprises a non-biological fluid.
92. The device of claim 85, wherein at least one of the fluid containing reservoirs contains a biomolecule.
93. The device of claim 85, wherein at least one of the fluid containing reservoirs contains a chemical or biological compound.
94. The device of claim 92, wherein the biomolecule is selected from the group consisting of nucleotides, peptides, oligomers, and polymers.
95. The device of claim 92, wherein the biomolecule is attached to a cell.
96. The device of claim 73, wherein the positioning means is adapted to repeatedly reposition the ejector so to enable ejection of a droplet from each of the reservoirs.

97. The device of claim 96, further comprising a substrate positioning means for positioning the substrate surface with respect to the ejector.

98. The device of claim 73, further comprising a means for maintaining a fluid in each reservoir at a constant temperature.

99. The device of claim 73, further comprising a temperature controlled coupling fluid provided between the ejector and each reservoir.

100. The device of claim 73, comprising a single ejector.

101. The device of claim 72, wherein the acoustic coupling relationship comprises positioning the ejector such that the acoustic radiation is generated and focused external to the reservoir.

102. The device of claim 101, wherein the acoustic coupling relationship between the ejector and the fluid in the reservoir is established by providing an acoustically conductive medium between the ejector and the reservoir.

103. The device of claim 71, wherein said ratio is greater than approximately 3:1.

104. The device of claim 71, wherein said ratio is no more than 4:1.

105. The device of claim 71, wherein said ratio is in the range of approximately 2.5:1 to approximately 3:1.

106. The device of claim 71, wherein said ratio is approximately 4:1.

107. The device of claim 71, comprising more than one thousand reservoirs.

108. The device of claim 71, comprising thousands of reservoirs.

109. The device of claim 71, comprising many thousands of reservoirs.

110. The device of claim 71, further comprising cooling means for lowering the temperature of the substrate surface.

111. The device of claim 88, wherein the nonaqueous fluid comprises an organic solvent.

112. The device of claim 88, wherein the nonaqueous fluid comprises a non-biological fluid.

113. A method for ejecting a fluid from a fluid reservoir toward designated sites on a substrate surface, comprising:

(a) providing a device comprised of:

(i) a reservoir containing a first fluid, said reservoir having an aperture that enables conduction of acoustic energy in a substantially uniform manner, said aperture having a selected cross-sectional width; and

(ii) an ejector comprised of an acoustic radiation generator for generating acoustic radiation and a focusing means capable of focusing the generated acoustic radiation to emit a droplet from a surface of the first fluid contained within the fluid reservoir, said surface being an effective distance from the aperture, wherein the ratio of the effective distance from the aperture to the cross-sectional width of the aperture is greater than about 2:1;

(b) positioning the ejector so as to be in acoustically coupled relationship to the fluid-containing reservoir, wherein the position of the ejector places the focusing means the effective distance away from the surface of the first fluid; and

(c) activating the ejector to generate acoustic radiation having a focal spot of a diameter  $D$  at the surface of the first fluid, thereby ejecting a droplet of the first fluid from the reservoir.

114. The method of claim 113, wherein said ratio is greater than approximately 3:1.

115. The device of claim 113, wherein said ratio is in the range of approximately 2.5:1 to approximately 3:1.
116. The method of claim 113, wherein said ratio is no more than 4:1.
117. The method of claim 113, wherein said ratio is approximately 4:1.
118. The method of claim 113, wherein the ejected droplet has a diameter less than the diameter of the focal spot.
119. The method of claim 118, wherein two droplets are ejected during step (c).
120. The method of claim 119, wherein the two ejected droplets are deposited as first and second droplets and the second droplet is larger than the first droplet.
121. The method of claim 119, wherein each of the ejected droplets has a width less than D.
122. The method of claim 113, wherein the device comprises a plurality of reservoirs each adapted to contain a fluid, and wherein the device is capable of ejecting a fluid droplet from each of the plurality of reservoirs toward a plurality of designated sites on the substrate surface and the method further comprises:
- (d) positioning the ejector so as to be in acoustically coupled relationship to a second fluid-containing reservoir containing a second fluid; and
  - (e) activating the ejector as in step (b) to eject a droplet of the second fluid from the second reservoir toward a second designated site on the substrate surface.
123. The method of claim 122, wherein each of the ejected droplets of the first fluid and second fluids has a width less than D.

124. The method of claim 122, wherein two droplets are ejected during at least one of steps (c) or (e).

125. The method of claim 124, wherein each of the two droplets ejected during step (c) or (e) has a width less than D.

126. The method of claim 124, wherein at least two ejected droplets are deposited at the same designated site on the substrate surface.

127. The method of claim 126, wherein the two ejected droplets are deposited as first and second droplets and the second droplet is larger than the first droplet.

128. The method of claim 122, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet size and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet of the desired size.

129. The method of claim 122, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet velocity and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet at the desired droplet velocity.

130. The method of claim 122, further comprising repeating steps (d) and (e) with one or more additional fluid-containing reservoirs.

131. The method of claim 122, wherein each of the ejected droplets has a volume of 5 pL.

132. The method of claim 122, wherein each of the ejected droplets has a diameter in the range of about 30 micrometers to about 60 micrometers.

133. The method of claim 122, wherein each of the ejected droplets has a diameter in the range of about 120 micrometers to about 250 micrometers.

134. The method of claim 122, wherein each of the ejected droplets has a diameter in the range of about 60 micrometers to about 500 micrometers.

135. The method of claim 122, wherein each of the ejected droplets has a diameter in the range of about 500 micrometers to about 1,000 micrometers.

136. The method of claim 122, wherein each of the ejected droplets has a diameter in the range of about 1 micrometer to about 10,000 micrometers.

137. The method of claim 122, wherein each of the ejected droplets has a diameter of less than about 10,000 micrometers.

138. The method of claim 122, further comprising, before each ejector activation step, measuring the fluid level in the reservoir in acoustically coupled relationship with the ejector.

139. The method of claim 138, wherein each measuring step is carried out acoustically.

140. The method of claim 139, wherein each measuring step is carried out using acoustic radiation from the ejector.

141. The method of claim 113, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet size and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet of the desired size.

142. The method of claim 113, wherein prior to step (c) an acoustic radiation tone burst duration is selected that is sufficient to achieve a desired droplet velocity and during step (c) the ejector is activated so as to generate a tone burst of acoustic radiation of the selected duration, thereby ejecting a droplet at the desired droplet velocity.